PHRM0002-105 PATENT

#6

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of: **Lowery, Smith, Kubiak and Larsen**

Serial No.: **10/523,893** Group Art Unit: **To Be Determined**

Filing Date: **Herewith** Examiner: **To Be Determined**

For: **Drosophila G Protein Coupled Receptors, Nucleic Acids and Methods Related to the Same**

EXPRESS MAIL LABEL NO: EV514684887US
DATE OF DEPOSIT: JUNE 15, 2005

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

INFORMATION DISCLOSURE STATEMENT

Pursuant to 37 C.F.R. §§ 1.56 and in accordance with 37 C.F.R. §§ 1.97 and 1.98, information relating to the above-identified application is hereby disclosed, the Examiner in charge of the above-identified application is requested to consider and make of record the references listed on the PTO Forms SB/08A and SB/08B, formerly known as PTO Form 1449 submitted herewith.

Inclusion of the information submitted herewith is not to be construed as an admission that the information is material as that term is defined in 37 C.F.R. § 1.56(b).

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made.

This Information Disclosure Statement is being filed:

☐ within three months of the filing date of the patent application.

☐ within three months of the date of entry into the national stage as set forth in 37 C.F.R. § 1.491 of the international application.

☒ **before** the mailing date of a first Office Action on the merits.

☐ **after** the mailing date of a first Office Action on the merits, but before the mailing date of a Final Office Action under 37 C.F.R. § 1.116 or a Notice of Allowance under 37 C.F.R. § 1.311, and accordingly is accompanied by:

☐ the Statement under 37 C.F.R. § 1.97(e) (see "Statement" below);

or

☐ the Fee of $180.00 set forth in 37 C.F.R. § 1.17(p); or

☐ No fee is owed by the applicant(s).

☐ In accordance with 37 C.F.R. § 1.129(a), this Information Disclosure Statement is being filed in connection with ☐ the first or ☐ second After Final Submission, and accordingly is accompanied by the Statement under 37 C.F.R. § 1.97(e) (see "Statement" below) and the fee of $180.00 as set forth in 37 C.F.R. § 1.17(p), is attached.

☐ **after** the mailing date of a Final Office Action under 37 C.F.R. § 1.116 or a Notice of Allowance under 37 C.F.R. § 1.311, but before the payment of the Issue Fee, and accordingly is accompanied by the Statement under 37 C.F.R. § 1.97(e), (see "Statement," and "Fees" below).

☐ Copies of the references listed on the attached PTO Forms SB/08a and SB/08b, formerly known as PTO Form 1449 are enclosed.

EXCEPT THAT:

☐ In view of the voluminous nature of reference @@, and the likelihood that this reference is available to the Examiner, copies are not enclosed herewith.

☒ In accordance with 37 C.F.R. § 1.98(d), copies of the following references listed on the attached PTO Form SB/08A and PTO Form SB/08B, formerly known as PTO Form 1449 are not enclosed herewith because they were previously cited by or submitted to the U.S. Patent and Trademark Office in patent application(s) for which a claim for priority under 35 U.S.C. § 120 have been made in the instant application.

☐ If any of the foregoing publications are not available to the Examiner, Applicant will endeavor to supply copies at the Examiner's request.

Statement under 37 C.F.R. § 1.97(e)

☐ The undersigned attorney hereby states that each item information contained in the Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign patent application not more than three months prior to the filing of the Information Disclosure Statement.

Fees

☒ No Fee is owed by the applicant(s).

☐ The Information Disclosure Statement Fee of $180.00 under 37 C.F.R. § 1.17(p) is enclosed herewith.

Method of Payment of Fees

☐ Attached is a check in the amount of $_____. This form is submitted in duplicate.

☐ Charge Deposit Account No. 50-1275 in the amount of $180.00. This form is submitted in duplicate.

☒ Please charge any deficiency or credit any overpayment to Deposit Account 50-1275.

☐ No fee or Statement is required under 37 C.F.R. § 1.97(b).

Respectfully submitted,

Gwilym J.O. Attwell
Registration No. 45,449

Dated: June 15, 2005

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PTO/SB/08a (08-03)
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Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 1 of 19

Complete if Known	
Application Number	10/526,893
Filing Date	Herewith
First Named Inventor	David E. Lowery
Art Unit	To Be Determined
Examiner Name	To Be Determined
Attorney Docket Number	PHRM0002-105

U.S. PATENT DOCUMENTS

Examiner Initials *	Cite No.[1]	Document Number: Number, Kind Code[2] (if known)	Publication/Issue Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	AA	US-4,343,940	8-10-1982	Kreighbaum et al.	
	AB	US-4,399,216	8-16-1983	Axel et al.	
	AC	US-4,447,608	5-08-1984	Jones et al.	
	AD	US-4,683,195	7-28-1987	Mullis et al.	
	AE	US-4,683,202	7-28-1987	Mullis	
	AF	US-4,757,072	7-12-1988	Kabbe et al.	
	AG	US-4,879,236	11-07-1989	Smith et al.	
	AH	US-5,217,999	6-08-1993	Levitzki et al.	
	AI	US-5,302,606	4-12-1994	Spada et al.	
	AH	US-5,316,553	5-31-1994	Kaul et al.	
	AK	US-5,330,992	7-19-1994	Eissenstat et al.	
	AL	US-5,585,277	12-17-1996	Bowie et al.	
	AM	US-5,753,615	5-19-1998	Thorpe et al.	
	AN	US-5,880,141	3-09-1999	Tang et al.	
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FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document: Country Code[3] - Number[4] - Kind Code[5] (if known)	Publication Date/Filing Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]
	AO	EP 0 367 566	05-1990	Immunex Corp		
	AP	EP 0 520 722	12-1992	Imperial Chem		
	AQ	EP 0 562 734	09-1993	Zeneca Ltd. et al.		
	AR	WO01/70981	9/27/01	Ebens et al		
	AS	WO 91/09955	07-1991	App. Research		
	AT	WO 91/15495	10-1991	Pfizer		
	AU	WO 91/18982	12-1991	Immunex Corp		
	AV	WO 92/20642	11-1992	Rhone-Poulenc		
	AW	WO 92/20808	11-1992	Cell Genesys		

Examiner Signature	/John Ulm/	Date Considered	04/05/07

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 2 of 19

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Application Number	10/526,893
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First Named Inventor	David E. Lowery
Art Unit	To Be Determined
Examiner Name	To Be Determined
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		US-			
		US-			
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FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[3] - Number[4] - Kind Code[5] (*if known*)	Publication Date/Filing Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]
	AX	WO 92/21660	12-1992	Pfizer		
	AY	WO 93/11236	06-1993	Med. Research Council		
	AZ	WO 94/03427	02-1994	Warner-Lambert		
	BA	WO 94/12650	06-1994	Transkaryotic		
	BB	WO 94/14808	07-1994	Farmitalia Carlo Erba S.R.L.		
	BC	WO 95/20652	08-1995	Medigene		
	BD	WO 96/22976	08-1996	Pharmacia SPA		
	BE	WO 97/09433	03-1997	Med. Research Counsil		
	BF	WO 98/37177	08-1998	MS State Univ.		
	IE	WO 01/71042	09-27-2001	PE Corp.		
	IF	WO01/75980	09/27/01	Cravchik		
	IG	EP 0 566 266	10-1993			

Examiner Signature	/John Ulm/	Date Considered	04/05/07

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This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 3 of 19

Complete if Known	
Application Number	10/526,893
Filing Date	Herewith
First Named Inventor	David E. Lowery
Art Unit	To Be Determined
Examiner Name	To Be Determined
Attorney Docket Number	PHRM0002-105

NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
	BG	Allen et al., "Modulation of CD4 by Suramin", Clin. Exp. Immunol., 1993, vol. 91, pp. 141-156.	
	BH	Altschul et al., "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs," Nucl. Acids Res., 1997, 25(17), 3389-3402.	
	BI	Altschul et al., "Basic Local Alignment Search Tool," J. Mol. Biol., 1990, 215, 403-410.	
	BJ	Anafi et al., "Tyrphostin-Induced Inhibition of p210.sup.bcr-abl Tyrosine Kinase Activity Induces K562 to Differentiate", Blood, 1993, vol. 82, No. 12, pp. 3524-3529.	
	BK	Anderson, W. F., "Human gene therapy," Science, 1992, 256, 808-813.	
	BL	Aukrust et al., "Enhanced Levels of Soluble and Membrane-Bound CD40 Ligand in Patients with Unstable Angina. Possible Reflection of T Lymphocyte and Platelet Involvement in the Pathogenesis of Acute Coronary Syndromes", Circulation, 1999, vol. 100, pp. 614-620.	
	BM	Ausubel, et al. (Eds.), "Chapter 6, Screening of recombinant DNA libraries," Current Protocols in Molecular Biology, 1994, John Wiley & Sons, 6.0.1-6.4.10.	
	BN	Baindur et al.,"Selective fluorescent ligands for pharmacological receptors," Drug Dev. Res., 1994, 33, 373-398.	
	BO	Baker et al., "Induction of Acetylcholine Receptor Clustering by Native Polystyrene Beads. Implication of an Endogenous Muscle-derived Signalling System", J. Cell. Sci., 1992, vol. 102, pp. 543-555.	
	BP	Barker et al., "In-Vitro Activity of Non-glutamate Containing Quinazoline-based Thymidylate Synthase Inhibitors", Proc. of Am. Assoc. for Cancer Res., 1991, vol. 32, p. 327.	
	BQ	Benoist et al., "In vivo sequence requirements of the SV40 early promoter region," Nature, 1981, 290, 304-310.	

Examiner Signature	/John Ulm/	Date Considered	04/05/07

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 4 of 19

Complete if Known	
Application Number	10/526,893
Filing Date	Herewith
First Named Inventor	David E. Lowery
Art Unit	To Be Determined
Examiner Name	To Be Determined
Attorney Docket Number	PHRM0002-105

NON PATENT LITERATURE DOCUMENTS

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	BR	Bertino, Cancer Res., "Toward Improved Selectivity in Cancer Chemotherapy: The Richard and Hinda Rosenthal Foundation Award Lecture", 1979, vol. 3, pp. 293-304.	
	BS	Bilder et al., "Tyrphostins Inhibit PDGF-induced DNA Synthesis and Associated Early Events in Smooth Muscle Cells", Amer. Physiol. Soc., 1991, pp. 6363-6143:C721-C730.	
	BT	Birgul, N. et al., "Reverse physiology in Drosophila: Identification of a novel allatostatin-like neuropeptide and its cognate receptor structurally related to the mammalian somatostatin/galanin/opioid receptor family", The EMBO Journal, 1999, 18(21), 5892-5900.	
	BU	Bohm, S. K., et al., "Regulatory mechanisms that modulate signalling by G-protein-coupled receptors," Biochem. J., 1997, 322, 1-18.	
	BV	Bosse, R., et al., "Development of nonseparation binding and functional assays for G protein-coupled receptors for high throughput screening: Pharmacological characterization of the immobilized CCR5 receptor on FlashPlate.RTM.," J. Biomolecular Screening, 1998, 3(4), 285-292.	
	BW	Boulton, T. G., et al., "ERKs: A family of protein-serine/threonine kinases that are activated and tyrosine phosphorylated in response to insulin and NGF," Cell, 1991, 65, 663-675.	
	BX	Brunton, V. G., et al., Proceedings of Amer. Assoc. Cancer Res., No. 3335, 1992, 33, 558.	
	BY	Bryckaert, M., et al., "Inhibition of platelet-derived growth factor-induced mitogenesis and tyrosine kinase activity in cultured bond marrow fibroblasts by tyrphostins," Experimental Cell Research, 1992, 199, 255-261.	
	BZ	Burke, T. R., et al., "Bicyclic compounds as ring-constrained inhibitors of protein-tyrosine kinase p56.sup.ick," J. Med. Chem., 1993, 36(4), 425-432.	
	CA	Burke, T. R., et al., "Arylamides of hydroxylated isoquinolines as protein-tyrosine kinaseinhibitors,"BioOrganic Med. Chem. Ltrs., 1992, 2(12), 1771-1774.	
	CB	Capecchi, M. R., "Altering the genome by homologous recombination," Science, 1989, 244, 1288-1292.	

Examiner Signature	/John Ulm/	Date Considered	04/05/07

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 5 of 19

Complete if Known	
Application Number	10/526,893
Filing Date	Herewith
First Named Inventor	David E. Lowery
Art Unit	To Be Determined
Examiner Name	To Be Determined
Attorney Docket Number	PHRM0002-105

NON PATENT LITERATURE DOCUMENTS

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	CC	Chambers, R. C., et al., "Thrombin stimulates fibroblast procollagen production via proteolytic activation of protease-activated receptor 1," Biochem J., 1998, 333, 121-127.	
	CD	Choo, Y., et al., "Promoter-specific activation of gene expression directed by bacteriophage-selected zinc fingers," J. Mol. Biol., 1997, 273, 525-532.	
	CE	Cicala, C., et al., "Bronchoconstrictor effect of thrombin and thrombin receptor activating peptide in guinea-pigs in vivo," Br. J. Pharmacol, 1999, 126, 478-484.	
	CF	Cirino, G., et al., "Thrombin functions as an inflammatory mediator through activation of its receptor," J. Exp. Med., 1996, 183, 821-827.	
	CG	Colotta, F., et al., "Expression of monocyte chemotactic protein-1 by monocytes and endothelial cells exposed to thrombin," Am. J. Pathol, 1994, 144, 975-985.	
	CH	Cosman, D., et al., "High Level Stable Expression of Human Interleukin-2 receptors in Mouse Cells Generates only Low Affinity Interleukin-2 Binding Sites," Mol. Immunol., 1986, 23(9), 935-941.	
	CI	Cosman, D., et al., "Cloning, sequence and expression of human interleukin-2 receptor," Nature, 1984, 312, 768-771.	
	CJ	Curtin, N. J., et al., "Inhibition of the growth of human hepatocellular carcinoma in vitro and in athymic mice by a quinazoline inhibitor of thymidylate synthase, CB3717," J. Cancer, 1986, 53, 361-368.	
	CK	Dayoff, in Atlas of Protein Sequence and Structure, 1972, National Biochemical Research Foundation, Washington, D.C., 5, 124.	
	CL	DiCuccio, M. N., et al., "A functional tethered ligand thrombin receptor is present on human hematopoietic progenitor cells," Exp. Hematol, 1996, 24, 914-918.	
	CM	Dolle, R. E., et al., "5,7-dimethoxy-3-(4-pyridinyl)quinoline is a potent and selective inhibitor of human vascular .beta.-type platelet-derived growth factor receptor tyrosine kinase," J. Med. Chem., 1994, 37, 2627-2629.	

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Sheet 6 of 19

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Application Number	10/526,893
Filing Date	Herewith
First Named Inventor	David E. Lowery
Art Unit	To Be Determined
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Attorney Docket Number	PHRM0002-105

NON PATENT LITERATURE DOCUMENTS

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	CN	Dong, Z., et al., "Activation of tumoricidal properties in macrophages by lipopolysaccharide requirements protein-tyrosine kinase activity," J. Leukocyte Biology, 1993, 53, 53-60.	
	CO	Dong, Z., et al., "Protein tyrosine kinase inhibitors decrease induction of nitric oxide synthase activity in lipopolysaccharide-responsive and lipopolysaccharide-nonresponsive murine macrophages," J. Immunol., 1993, 151(5), 2717-2724.	
	CP	Donovan, F. M., et al., "Thrombin induces apoptosis in cultured neurons and astrocytes via a pathway requiring tyrosin kinase and RhoA activities," J. Neurosci., 1997, 17(14), 5316-5326.	
	CQ	Dooley, C. T., et al., "Binding and in vitro activities of peptides with high affinity for the nociceptin/orphanin FQ receptor, ORL1," J. Pharmacology and Experimental Therapeutics, 1997, 283(2), 735-741.	
	CR	Dunlop, J., et al., "Characterization of 5-HT.sub.1A receptor functional coupling in cells expressing the human 5-HT.sub.1A receptor as assessed with the cytosensor microphysiometer," J. Pharmacological and Toxicological Methods, 1998, 40(1), 47-55.	
	CS	Fernandes, D. J., et al., "Biochemical and antitumor effects of 5,8-dideazaisopteroylglutamate, a unique quinazoline inhibitor of thymidylate synthase," Cancer Research, 1983, 43, 1117-1123.	
	CT	Ferris, J. P., et al., "Synthesis of Quinazoline Nucleosides from Ribose and Anthranilonitrile. Application of Phase-Transfer Catalysis in Nucleoside Synthesis," J. Org. Chem., 1979, 44(2), 173-178.	
	CU	Fields, S., et al., "A novel genetic system to detect protein-protein interactions," Nature, 1989, 340, 245-246.	
	CV	Fields, S., et al., "The two-hybrid system: an assay for protein-protein interactions," Trends in Genetics, 1994, 10, 286-292.	
	CW	Foote, J., et al., "Antibody framework residues affecting the conformation of the hypervariable loops, J. Mol. Biol., 1992, 224, 487-499.	
	CX	Frandsen, E. K., et al., "A simple ultrasensitive method for the assay of cyclic AMP and CMP in tissues," Life Sciences, 1976, 529-542.	

Examiner Signature	/John Ulm/	Date Considered	04/05/07

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 7 of 19

Complete if Known	
Application Number	10/526,893
Filing Date	Herewith
First Named Inventor	David E. Lowery
Art Unit	To Be Determined
Examiner Name	To Be Determined
Attorney Docket Number	PHRM0002-105

NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
	CY	Fry, D.W., et al., "A specific inhibitor of the epidermal growth factor receptor tyrosine kinase," Science, 1994, 265, 1093-1095.	
	CZ	Gazit, A., et al., "Tyrphostins I: Synthesis and biological activity of protein tyrosine kinase inhibitors," J. Med. Chem., 1989, 32, 2344-2352.	
	DA	Gazit, A., et al., "Tyrphostins. 3. Structure-activity relationship studies of .alpha.-substituted benzylidenemalononitrile 5-S-aryltyrphostins," J. Med. Chem., 1993, 36, 3556-3564.	
	DB	George, S. E., et al., "Evaluation of a CRE-directed luciferase reporter gene assay as an alternative to measuring cAMP accumulation," J. Biomolecular Screening, 1997, 2(4), 235-240.	
	DC	Gerhardt, C. C., et al., "Functional characteristics of heterologously expressed 5-HT receptors," Eur. J. Pharmacology, 1997, 334, 1-23.	
	DD	Gill, J. S., et al., "Thrombin induced inhibition of neurite outgrowth from dorsal root ganglion neurons," Brain Res., 1998, 797, 321-327.	
	DE	Grabham, P., et al., Thrombin receptor activation stimulates astrocyte proliferation and reversal of stellation by distinct pathways: involvement of tyrosine phosphorylation, J. Neurochem, 1995, 64, 583-591.	
	DF	Greisman, H. A., et al., "A general strategy for selecting high-affinity zinc finger proteins for diverse DNA target sites," Science, 1997, 275, 657-661.	
	DG	Guerrero, F. D., "Transcriptional Expression of a Putative Tachykinin-like Peptide Receptor Gene From Stable Fly.sup.1," Peptides, 1997, 18(1), 1-5.	
	DH	Hauck, R. W., et al., ".alpha.-thrombin stimulates contraction of human bronchial rings by activation of protease-activated receptors," Am J. Physiol, 1999, 277, L22-L29.	
	DI	Hauser, F., et al., "Molecular Cloning, Genomic Organization, and Developmental Regulation of a Novel Receptor from Drosophila melanogaster Structurally Related to Members of the Thyroid-stimulating Hormone, Follicle-stimulating Hormone, Luteinizing Hormone/ Choriogonadotropin Receptor Family from Mammals," The J. of Biological Chemistry, 1997, 272(2), 1002-1010.	

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	DJ	Hauser, F. et al., "Molecular Cloning, Genomic Organization, and Developmental Regulation of a Novel Receptor from Drosophila melanogaster Structurally Related to Gonadotropin-Releasing Hormone Receptors from Vertebrates," Biochem. Biophys. Res. Comm., 1998, 249, 822-828.	
	DK	Henikoff, S., et al., "Amino acid substitution matrices from protein blocks," Proc. Natl. Acad. Sci. USA, 1992, 89, 10915-10919.	
	DL	Hill, D. C., "Trends in development of high-throughput screening technologies for rapid discovery of novel drugs," Cur. Opinion Drug Disc. Dev., 1998, 1(1), 92-97.	
	DM	Hodgson, J., "Receptor screening and the search for new pharmacteuticals," Bio/Technology, 1992, 10, 973-980.	
	DN	Hoffman, M., et al., "Thrombin enhances monocyte secretion of tumor necrosis factor and interleukin-1 beta by two distinct mechanisms," Blood Cells Mol Dis, 1995, 21, 156-167.	
	DO	Jackman, A. L., et al., "ICID1694, a quinazoline antifolate thymidylate synthase inhibitor that is a potent inhibitor of L1210 tumor cell growth in vitro and in vivo: A new agent for clinical study," Cancer Research, 1981, 51, 5579-5586.	
	DP	Jayawickreme, C. K., et al., Gene expression systems in the development of high-throughput screens, Current Opinion in Biotechnology, 1997, 8, 629-634.	
	DQ	Jones, P. T., et al., "Replacing the compementarity-determining regions in a human antibody with those from a mouse," Nature, 1986, 321, 522-525.	
	DR	Jones, T. R., et al., "Quinazoline Antifolates Inihibiting Thymidylate Synthase: Variation of the Amino Acid," J. Med Chem., 1986, 29, 1114-1118.	
	DS	Kanterman, R. Y., et al., "Transfected D.sub.2 dopamine receptors mediate the potentiation of arachidonic acid release in chinese hamster ovary cells," Molecular Pharmacology, 1991, 39, 364-369.	
	DT	Karlin, S., et al., "Applications and statistics for multiple high-scoring segments in molecular sequences," Proc. Natl. Acad. Sci. USA, 1993, 90, 5873-5787.	

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	DU	Kaur, G., et al., "Tyrphostin induced growth inhibition: corelation with effect on p210.sup.ber-abl autokinase activity in K562 chronic myelogenous leukemia," Anti-Cancer Drugs, 1994, 5, 213-222.	
	DV	Kettleborough, C. A., et al., "Humanization of a mouse monoclonal antibody by CDR-grafting: the importance of framework residues on loop conformation," Protein Engin., 1991, 4(7), 773-783.	
	DW	Kim, J., et al., "Design of TATA box-binding protein/zinc finger fusions for targeted regulation of gene expression," Proc. Natl. Acad. Sci. USA, 1997, 94, 3616-3620.	
	DX	King, M. J., et al., "Site-specific dephosphorylation and deactivation of the human insulin receptor tyrosine kinase by particulate and soluble phosphotyrosyl protein phosphatases," Biochem. J., 1991, 275, 413-418.	
	DY	Kowal, D., et al., "A [.sup.35 S]GTP.gamma.S binding assessment of metabotropic glutamate receptor standards in chinese hamster ovary cell lines expressing the human metabotropic receptor subtypes 2 and 4," Neuropharmacology, 1998, 37, 179-187.	
	DZ	Kuntzweiler, T. A., et al., "Rapid assessment of ligand actions with nicotinic acetylcholine receptors using calcium dynamics and FLIPR," Drug Development Research, 1998, 44(1), 14-20.	
	EA	Kuo, M., et al., "Effects of signalling transduction modulators on the transformed phenotypes in v-H-ras-transformed NIH3T3 cells," Cancer Letters, 1993, 74, 197-202.	
	EB	Lajiness et al., "D2 dopamine receptor stimulation of mitogenesis in transfected chinese hamster ovary cells: relationship to dopamine stimulation of tyrosine phosphorylations", J. Pharm. Exp. Ther., 1993, vol. 267, No. 3, 1573-1581.	
	EC	Lee, C., et al., "Active-site directed reductive alkylation of xanthine oxidase by imidazo[4,5-g]quinazoline-4,9-diones functionalized with a leaving group," Biochemistry, 1987, 26(23), 7355-7362.	
	ED	Lehninger, "Chapter 4, The amino acid building blocks of proteins," Biochemistry, 2.sup.nd Ed., 1975, Worth Publishers, Inc., New York, New York, 71-77.	
	EE	Lemus, et al., "Studies of extended quinone methides. Synthesis and physical studies of purine-like monofunctional and bifunctional imidazo[4,5-g]quinazoline reductive alkylating agents," J. Org. Chem., 1989, 54, 3611-3618.	

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Sheet 10 of 19

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First Named Inventor	David E. Lowery
Art Unit	To Be Determined
Examiner Name	To Be Determined
Attorney Docket Number	PHRM0002-105

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	EF	Lenz, C. et al., "Molecular Cloning and Genomic Organization of a Second Probable Allastatin Receptor from Drosophila melanogaster", Biochem. Biophys. Res. Comm., 2000, 273, 571-577.	
	EG	Lenz, C. et al., Drosophila melanogaster allatostatin G-protein receptor mRNA, complete cds, GenBank Accession No. AF253526, Jul. 14, 2000.	
	EH	Lenz, C. et al., "Molecular Cloning and Genomic Organization of an Allatostatin Preprohormone from Drosophila melanogaster", Biochem. Biophys. Res. Comm., 2000, 273, 1126-1131.	
	EI	Levitzki, A., "Tyrphostins: tyrosine kinase blockers as novel antiproliferative agents and dissectors of signal transduction," The FASEB J., 1992, 6, 3275-3282.	
	EJ	Ley, K., et al., "Synthesen unter verwendung von benzofuroxan," Synthesis, 1975, 415-522 (English abstract).	
	EK	Li, X-J., et al., "Cloning, heterologous expression and developmental regulation of a Drosophila receptor for tachykinin-like peptides," The EMBO Journal, 1991, 10(11), 3221-3229.	
	EL	Li, X-J., et al., "Cloning, Functional Expression and Developmental Regulation of a Neuropeptide Y Receptor from Drosophila melanogaster," The J. of Biological Chemistry, 1992, 267(1), 9-12.	
	EM	Li, X.-J. et al., D. melanogaster neuropeptide receptor mRNA, complete cds, GenBank Accession No. M81490, Apr. 28, 1993.	
	EN	Lin, A. H., et al., "The oxazolidinone eperezolid binds to the 50S ribosomal subunit and competes with binding of chloramphenicol and lincomycin," Antimicrobial Agents and Chemotherapy, 1997, 41(10), 2127-2131.	
	EO	Liu, Q., et al., "Design of polydactyl zinc-finger proteins for unique addressing within complex genomes," Proc. Natl. Acad. Sci. USA, 1997, 94, 5525-5530.	
	EP	Luckow, V. A., et al., "High Level Expression of Nonfused Foreign Genes with Autographa californica Nuclear Polyhedrosis Virus Expression Vectors," Virology, 1989, 170, 31-39.	

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	EQ	Luckow, V. A., et al., "Trends in the development of baculovirus expression vectors," Bio/Technology, 1988, 6, 47-55.	
	ER	Lyall, R. M., et al., "Tyrphostins inhibit epidermal growth factor (EGF) receptor tyrosine kinase activity in living cells and EGF-stimulated cell preliferation," J. Biol. Chem., 1989, 264, 14503-14509.	
	ES	Maguire, M. P., et al., "A new series of PDGF receptor tyrosine kinase inhibitors: 3-substituted quinoline derivatives," J. Med. Chem., 1994, 37, 2129-2131.	
	ET	Maxwell, R. J., et al., ".sup.19 F nuclear magnetic resonance imaging of drug distribution in vivo: The disposition of an antifolate anticancer drug in mice," Magnetic Resonance in Medicine, 1991, 17, 189-196.	
	EU	McColl, D. J., et al., "Structure-based design of an RNA-binding zinc finger", Proc. Natl. Acad. Sci. (USA), 1997, vol. 96, 9521-9526.	
	EV	Mini, E., et al., "Cytotoxic effects of folate antagonists against methotrexate-resistant human leukemic lymphoblast CCRF-CEM cell lines," Cancer Res., 1985, 45, 325-330.	
	EW	Monnier, D., et al., "NKD, a Developmentally Regulated Tachykinin Receptor in Drosophila," The J. of Biological Chemistry, 1992, 267(2), 1298-1302.	
	EX	Monnier, D. et al., Drosophila melanogaster tachykinin receptor (NKD) mRNA, complete cds, GenBank Accession No. M77168, Apr. 26, 1993.	
	EY	Morris, R., et al., "Thrombin receptor expression in rheumatoid and osteoarthritic synovial tissue", Ann. Rheum. Dis., 1996, vol. 55, 841-843.	
	EZ	Morrison, et al., "Genetically engineered antibody molecules," Dixon, F.J., et al. (Eds.), Adv. Immunol., 1989, 44, 65-92.	
	FA	Murphy, A. J., et al., "From DNA to drugs: the orphan G-protein coupled receptors," Cur. Opinion Drug Disc. Dev., 1998, 1(2), 192-199.	

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	FB	Myers, P., "Will combinatorial chemistry deliver real medicines," Curr. Opin. Biotechnology, 1997, 8, 701-707.	
	FC	Nachman & Homan, in Insect Neuropeptides; Chemistry, Biology and Action, Menn, Kelly & Massler, Eds., 1991, 194-214, American Chemical Society, Washington, DC.	
	FD	Nakayama, G. R., "Microplate assays for high-throughput screening," Cur. Opinion Drug Disc. Dev., 1998, 1, 85-91.	
	FE	Naldini, A., et al., "Thrombin modulation of natural killer activity in human peripheral lymphocytes," Cell Immunol, 1996, 172, 35-42.	
	FF	Nambu et al., "Isolation and Characterization of a Drosophila Neuropeptide Gene", Neuron, 1988, 1, 55-61.	
	FG	Nichols, R. et al., "Identification and Characterization of a Drosophila Homologue to the Vertebrate Neuropeptide Cholecystokinin", J. Biol. Chem., 1988, 263, 12167-12170.	
	FH	Okayama, H., et al., "A cDNA cloning vector that permits expression of cDNA inserts in mammalian cells," Mol. Cell. Biol., 1983, 3(2), 280-289.	
	FI	Padlan, E. A., "A possible procedure for reducing the immunogenicity of antibody variable domains while preserving their ligand-binding properties," Molecular Immunol., 1991, 28(4/5), 489-498.	
	FJ	Pausch, M. H., "G-protein-coupled receptors in Saccharomyces cerevisiae: high-throughput screening assays for drug discovery," Trends in Biotechnology, 1997, 15, 487-494.	
	FK	Peterson, G., et al., "Genistein and biochanin A inhibit the growth of human prostate cancer cells but not epidermal growth factor receptor tyrosine autophosphorylation," The Prostate, 1993, 22, 335-345.	
	FL	Phillips, S. D., et al., "Quino[1,2-c]quinazolines. I. Synthesis of quino[1,2-c]quinazolinium derivatives and the related indazolo[2,3-a]quinoline derivatives as analogs of the antitumor benzol[c]phenanthridine alkaloids," J. Heterocyclic Chem., 1980, 17(19), 1589-1596.	

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	FM	Pillemer, G., et al., "Insulin dependence of murine lymphoid T-cell leukemia," Int. J. Cancer, 1992, 50, 80-85.	
	FN	Pindon, A., et al., "Thrombin-induced reversal if astricyte stellation is mediated by activation of protein kinase C beta.-1," Eur. J. Biochem., 1998, 255, 766-774.	
	FO	Posner, I., et al., "Kinetics of inhibition by tyrophostins of the tyrosine kinase activity of the epidermal growth factor receptor and analysis," Molecular Pharmacology, 1993, 45, 673-683.	
	FP	Reece, P. A., et al., "Pharmacokinetics of trimetrexate administered by five-day continuous infusion to patients with advanced cancer," Cancer Research, 1977, 47(11), 2996-2999.	
	FQ	Rendu, F., et al., "Inhibition of platelet activation by tyrosine kinase inhibitors," Biol. Pharmacology, 1992, 44(5), 881-888.	
	FR	Riechmann, L., et al., "Reshaping human antibodies for therapy," Nature, 1988, 332, 323-327.	
	FS	Rogers, M. V., "Light on high-throughput screening: fluorescence-based assay technologies," Drug Discovery Today, 1997, 2(4), 156-160.	
	FT	Sauro, M. D., et al., "Tyrphostin attenuates platelet-derived growth factor-induced contraction in aortic smooth muscle through inhibition of protein tyrosine kinase(s)," J. Pharm. And Experimental Therapeutics, 1993, 267(3), 1119-1125.	
	FU	Schroeder, K. S., et al., "FLIPR: A new instrument for accurate, high throughput optical screening," J. Biomolecular Screening, 1996, 1, 75-80.	
	FV	Schroeder, K. S., et al., "FLIPR: A new instrument for accurate, high throughput optical screening," J. Biomolecular Screening, 1996, 1, 75-80.	
	FW	Schroeder, K. S., et al., "FLIPR: A new instrument for accurate, high throughput optical screening," J. Biomolecular Screening, 1996, 1, 75-80.	

Examiner Signature	/John Ulm/	Date Considered	04/05/07

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 14 of 19

Complete if Known	
Application Number	10/526,893
Filing Date	Herewith
First Named Inventor	David E. Lowery
Art Unit	To Be Determined
Examiner Name	To Be Determined
Attorney Docket Number	PHRM0002-105

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	FX	Segal, D. J., et al., "Toward controlling gene expression at will: Selection and design of zine finger domains recognizing each of the 5'-GNN-3' DNA target sequences," Proc. Natl. Acad. Sci. USA, 1999, 96, 2758-2763.	
	FY	Sikora, E., et al., "Quinazoline CB 3717 and CB 3703 inhibition of folate retention and metabolism in ehrlich ascites carcinoma cells and some organs of the host-mouse," Cancer Letters, 1984, 23, 289-295.	
	FZ	Sikora, E., et al., "Development of an assay for the estimation of N.sup.10 -propargyl-5,8-dideazafolic acid polyglutamates in tumor cells," Analytical Biochemistry, 1988, 172, 344-355.	
	GA	Sim, L. J., et al., "Identification of opioid receptor-like (ORL1) peptide-stimulated [.sup.35 S]GTP.gamma.S binding in rat brain," Neuroreport, 1996, 7, 729-733.	
	GB	Smith, T. F., et al., "Comparison of biosequences," Adv. Appl. Math., 1981, 2, 482-489.	
	GC	Smith-Swintosky, V. L., et al., "Protease-activated receptor-2 (PAR-2_is present in the rat hippocampus and is associated with neurodegeneration," J. Neurocham, 1997, 69, 1890-1896.	
	GD	Stables, J., et al., "A bioluminescent assay for agonist activity at potentially any G-protein-coupled receptor," Analytical Biochemistry, 1997, 252, 115-126.	
	GE	Stratowa, C., et al., "Use of a luciferase reporter system for characterizing G-protein-linked receptors," Current Opinion in Biotechnology, 1995, 6, 574-581.	
	GF	Strosberg, et al., "Functional expression of receptors in microorganisms," Trends in Pharmacological Sciences, 1992, 13, 95-98.	
	GG	Strosberg, A. D., et al., "Structure/function relationship of proteins belonging to the family of receptors coupled to GTP-binding proteins,," Eur. J. Biochem., 1991, 196, 1-10.	
	GH	Suidan, H. A., et al., "The thrombin receptor in the nervous system," Semin Thromb Hemost, 1996, 22(2), 125-133.	
	GI	Sutherland, E. W., et al., "Some aspects of the biological role of adenosine 3',5'-monophosphate (cyclic AMP)," Circulation, 1968, 37, 279-306.	

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	GJ	Sweetnam, P. M., et al., "The role of receptor binding in drug discovery," J. Natural Products, 1993, 56(4), 441-455.	
	GK	Tempest, P. R., et al., "Reshaping a human monoclonal antibody to inhibit human respiratory syncytial virus infection in vivo," Bio/Technology, 1991, 9, 266-271.	
	GL	Torfs, H. et al., "Characterization of a receptor for insect tachykinin-like peptide agonists by functional expression in a stable Drosophila Schneider 2 Cell Line", J. Neurochem., 2000, 74, 2182-2189.	
	GM	Trejo, J., et al., "The cloned thrombin receptor is necessary and sufficient for activation of mitogen-activated protein kinase and mitogenesis in mouse lung fibroblasts," J. Biol. Chem., 1996, 271, 21536-21541.	
	GN	Turgeon, V. L., et al., "Thrombin perturbs neurite outgrowth and induces apoptotic cell death in enriched chick spinal motoneuron cultures through caspase activation," J. Neurosci, 1998, 18(17), 6882-6891.	
	GO	Ubl, J. J., et al., "Characteristics of thrombin-induced calcium signals in rat astrocytes," Glia, 1997, 21, 361-369.	
	GP	Vanden Broeck, "G-protein-coupled receptors in insect cells", Int. Rev. Cytology, 1996, 164, 189-268.	
	GQ	Verhoeyen, M., et al., "reshaping human antibodies: Grafting an antilysozyme activity," Science, 1988, 239, 1534-1536.	
	GR	Voet et al. Biochemistry. 1990. John Wiley & Sons, Inc.. pp. 126-128 and 228-234.	
	GS	Wieboldt, R., et al., "Immunoaffinity ultrafiltration with ion spray HPLC/MS for screening small-molecule libraries," Anal. Chem., 1997, 69(9), 1683-1691.	
	GT	Williams, M., "Receptor binding in the drug discovery process," Medicinal Research Reviews, 1991, 11(2), 147-184.	

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	GU	Wolbring, G., et al., "Inhibition of GTP-utilizing enzymes by tyrphostins," J. Biol. Chem., 1994, 269(36), 22470-22472.	
	GV	Wu, H., et al., "Building zinc fingers by selection: toward a therapeutic application," Proc. Natl. Acad. Sci. USA, 1995, 92, 344-348.	
	GW	Yoneda, T., et al., "The antiproliferative effects of tyrosine kinase inhibitors tyrphostins on a human squamous cell carcinoma in vitro and in nude mice," Cancer Research, 1991, 51, 4430-4435.	
	GX	Adams, M.D., et al., "The genome sequence of drosophila melanogaster," EMBL/GenBank/DDBJ, XP-002176201, Mar. 21, 2000, 3 pages.	
	GY	Alcedo, J., et al., "The drosophila smoothened gene encodes a seven-pass membrane protein, a putative receptor for the hedgehog signal," Cell, XP-002166694, Jul. 26, 1996, 86, 221-232.	
	GZ	Celniker, S.E., et al., "Drosophila melanogaster, chromosome X, region 17C-17E," EMBL, XP-002176202, Oct. 22, 1999, 2 pages.	
	HA	Celniker, S.E., et al., "Drosophila melanogaster, chromosome 2R, region 42A8-42A16, P1 clones DS06954 and DS05325," EMBL, XP-002176200, Mar. 24, 1999, 2 pages.	
	HB	Celniker, S.E., et al., "Drosophila melanogaster, chromosome 3R, region 83D-83D, BAC clone BACR26C09," EMBL, XP-002176198, Sep. 17, 1999, 2 pages.	
	HC	Muzny, D.M., et al., "Drosophila melanogaster clone RPC198-10L1," EMBL, XP-002166695, Aug. 23, 1999, 3 pages.	
	HD	Muzny, D.M., et al., "Drosophila melanogaster clone RPCI98-23M20," EMBL, xP-002176199, Aug. 23, 1999, 3 pages.	
	HE	Nichols, R., "Isolation and structural characterization of drosophila TDVDHVFLRF amide and FMRF amide-containing neural peptides," Medline, XP-002166696, 1992, 1 page.	

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	HF	Taghert, P.H., et al., "Interspecific comparison of a drosophila gene encoding FMRF amide-related neuropeptides," J. Neuroscience, USA,, 1990, 10(6), 1929-1942.	
	HG	Copy of PCT International Search Report dated Oct. 29, 2001 for International Application No. PCT/US00/29002.	
	*HI	Berger et al., "Guide to Molecular Cloning Techniques," *Methods in Enzymology*, Academic Press, Inc., San Diego, CA 1987.	
	*HI	Cobbold et al., "Aequorin measurements of cytoplasmic free calcium," McCormack J.G., et al. (Eds.), *Cellular Calcium: A Practical Approach* (1991) Oxford, IRL Press.	
	*HJ	*Current Protocols in Molecular Biology*, John Wiley & Sons, NY 1999.	
	*HK	Eisenthal et al., *Enzyme Assays: A Practical Approach*, Oxford University Press, 1992.	
	*HL	Harlow et al., *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 1988.	
	*HM	Haugland, *Handbook of Fluorescent Probes and Research Chemicals*, 6th Ed., 1996, Eugene OR: Molecular Probes.	
	*HN	Hendix, (ed.), *Lambda II*, Cold Spring Harbor Press, Cold Spring Harbor, NY 1980.	
	*HO	Hershey (ed.), *The Bacteriophage Lambda*, Cold Spring Harbor Press, Cold Spring Harbor, NY, 1973.	
	*HP	Kruse et al. (eds). *Tissue Culture*, Academic Press, 1973.	

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	HQ	O'Rielly et al. (eds.), *Baculovirus Expression Vectors: A Laboratory Manual*, W.H. Freeman and Company, New York, 1992.	
	HR	Sambrook et al., *Molecular Cloning: A Laboratory Manual*, second edition, Cold Spring Harbor Press, Cold Spring Harbor, NY 1989.	
	HS	Stapleton et al., "A *Drosophila* full-length cDNA Resource," *Genome Biology* (2002) 3(12):1-8.	
	HT	International Search Report dated April 19, 2004 for International Application No. PCT/US03/24488.	
	HU	Garcynski, et al., "Characterization of a functional neuropeptide F receptor from Drosophila melanogaster," Peptides (2002) 23:773-780	
	HV	Holmes, et al., "Cloning and transcriptional expression of leucokinin-like peptide receptor from the Southern cattle tick, Boophilus microplus (Acari:Ixodidae)," Insect Mol. Biol. (2000) 9:457-465	
	HW	Birgul, et al., "Reverse physiology in Drosophila: identification of a novel allatostatin-like neuropeptide and its cognate receptor structurally related to the mammalian somatostatin/galanin/opiod receptor family," EMBO J. 18:5892-5900	
	HX	Cazzamali, et al., "Molecular cloning and functional expression of a Drosophila corazonin receptor," Biochem. Biophys. Res. Comm. (2002) 298:31-36	
	HY	Larsen, et al., "Type A allatostatinsfrom Drosophila melanogaster and Diplotera punctata activate two Drosophila allatostatin receptors, DAR-1 and DAR-2, expressed in CHO cells," Biochem. Biophys. Res. Comm. (2001) 286:895-901	
	HZ	Nichols, "Isolation and expression of the Drosophila drosufakinin neural peptide gene product DSK-I," Mol. Cell. Neurosci. (1992) 3:342-347	
	IA	O'Donnell, et al., "Hormonally controlled chloride movement across Drosophila tubules is via ion channels in stellate cells," Am. J. Physiol. (1998) 43:R1039-R1049	

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	IB	Mertens, et al., "Characterization of the short neuropeptide F receptor from Drosophila melanogaster," Biochem. Biophys. Res. Comm. (2002) 1140-1148	
	IC	Siviter, et al., "Expression and functional characterization of a Drosophila neuropeptide precursor with homology to mammalian preprotachykinin A," J. Biol. Chem. (2000) 275:23273-23280	
	ID	Staubli, et al., "Molecular identification of the insect adipokinetic hormone receptors," Proc. Natl. Acad. Sci. USA (2002) 99:3446-3451	
	IE	Price et al., "Drosophila melanogaster flatline encodes a myotropin orthologue to Manduca sexta allatostatin," Peptides (2002) 23:787-794	
	IF	Kubiak, et al., "Cloning and Functional Expression of the first Drosophila melanogaster sulfakinin receptor DSK-R1," Biochem. Biophys. Res. Comm. (2002) 291:313-320	
	IG	Radford, et al., "Systematic G-protein-coupled receptor analysis in Drosophila melanogaster identifies a leucokinin receptor with novel roles," J. Biol. Chem. (2002) 277:38810-38817	
	IH	Williamson, et al, "Molecular cloning, genomic organization, and expression of a C-type (Manduca sexta-type) allatostatin preprohormone from Drosophila melanogaster," Biochem. Biophys. Res. Comm. (2001) 282:1124-130	
	II	Cazzamali, et al., "Molecular cloning and functional expression of the first insect FMRFamide receptor," Proc. natl. Acad. Sci. USA (2002) 99:12073-12078	
	IJ	Kreikenkamp et al., "Functional annotation of two orphan G-protein-coupled receptors, drostar1 and -2, from Drosophila melanogaster and their ligands by reverse pharmacology," J. Biol. Chem. (2002) 277:39937-39943	
	IK	Park et al., "Identification of G protein-coupled receptors for Drosophila PRXamide peptides, CCAP, corazonin, and AKH supports a theory of ligand-receptor coevolution," Proc. Natl. Acad. Sci. USA (2002) 99:11423-11428	

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